ORIGINAL ARTICLE

Defining and investigating occupational asthma: a consensus approach

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Background: At present there is no internationally agreed definition of occupational asthma and there is a lack of guidance regarding the resources that should be readily available to physicians running specialist occupational asthma services.
Aims: To agree a working definition of occupational asthma and to develop a framework of resources necessary to run a specialist occupational asthma clinic.
Method: A modified RAND appropriateness method was used to gain a consensus of opinion from an expert panel of clinicians running specialist occupational asthma clinics in the UK.
Results: Consensus was reached over 10 terms defining occupational asthma including: occupational asthma is defined as asthma induced by exposure in the working environment to airborne dusts vapours or fumes, with or without pre-existing asthma; occupational asthma encompasses the terms ''sensitiser-induced asthma'' and ''acute irritant-induced asthma'' (reactive airways dysfunction syndrome (RADS)); acute irritant-induced asthma is a type of occupational asthma where there is no latency and no immunological sensitisation and should only be used when a single high exposure has occurred; and the term ''work-related asthma'' can be used to include occupational asthma, acute irritant-induced asthma (RADS) and aggravation of pre-existing asthma. Disagreement arose on whether low dose irritant-induced asthma existed, but the panel agreed that if it did exist they would include it in the definition of ''work-related asthma''. The panel agreed on a set of 18 resources which should be available to a specialist occupational asthma service. These included pre-bronchodilator FEV_1 and FVC (% predicted); peak flow monitoring (and plotting of results, OASYS II analysis); non-specific provocation challenge in the laboratory and specific IgE to a wide variety of occupational agents.
Conclusion: It is hoped that the outcome of this process will improve uniformity of definition and investigation of occupational asthma across the UK.

Occupational asthma is the most common form of occupational lung disease in industrialised nations and causes significant morbidity and disability. Meta-analysis of studies estimating the proportion of cases of asthma in adults of working age to which occupational factors have contributed, have shown an attributable risk of between 9% and 15%.[1] At present there is no internationally agreed definition of occupational asthma. More importantly perhaps, in the UK there is no standard approach to investigating or managing these patients.

All definitions of occupational asthma specify that the causal agent should be specific to the workplace[2–8] and early definitions also stipulated that there should also be a sensitising mechanism.[5–7] However, evidence of sensitisation is only found in a minority of cases and occupational exposures can cause asthma without immune sensitisation (reactive airways dysfunction syndrome). An alternative, more pragmatic approach has been taken, with two types of occupational asthma being proposed, distinguishable by whether or not there is a latent period between exposure and symptoms.[9] The first type (also termed ''allergic'') appears following a latency period and the allergic mechanisms responsible may or may not yet be fully characterised. The second type (''non-allergic'') encompasses irritant induced asthma or reactive airways dysfunction syndrome (RADS).[9] Recently published evidence-based guidelines for the identification, management and prevention of occupational asthma[1] also proposes two types of occupational asthma and avoids implying a specific immunological mechanism. The authors define occupational asthma as being either ''hypersensitivity induced occupational asthma'' (characterised by a latency period and non-irritant mechanism) or ''irritant induced occupational asthma'' (due to an irritant mechanism and not requiring a latent interval). Increases in asthma symptoms, or re-activation of quiescent asthma in individuals with pre-existing asthma due to workplace exposure are normally excluded by definitions of occupational asthma. A variety of terms are used to define this concept, such as ''work aggravated asthma''.[10]

Consensus techniques have helped to improve the diagnosis and management of asthma in recent years[11] and are particularly useful in situations where the evidence base is sparse or undecided.[12–14] These techniques focus on exploring consensus among a group of experts by synthesising opinions in combination with available evidence. Consensus techniques are also becoming an increasingly important mechanism for developing quality tools.[15]

The aim of this study was to use a consensus technique in an attempt to agree a working definition for occupational asthma in the UK and to develop indicators of good practice in the investigation of patients with suspected occupational asthma.

METHODS

A modified RAND appropriateness method[16 17] was used for this study, which has been described as the only systematic method of combining expert opinion and evidence.[13] It combines

Abbreviation: RADS, reactive airways dysfunction syndrome

characteristics of both the Delphi Technique (eg, postal questionnaire) and the Nominal Group Technique (eg, face-to-face meeting).[15] The RAND appropriateness method is a dynamic process which allows the stem questions and scoring scales to be clarified or modified and extra indicators to be added up to the point of the final scoring at the panel meeting. This ensures that any ambiguities of meaning and important omissions are minimised, as recommended by Baker.[18] This method has been used previously to develop a set of quality indicators for the definition and investigation of difficult asthma.[19] Panel sizes of 9–12 members provide results that have been shown to be reproducible by second panels.[20] while facilitating group discussion and preventing the group from becoming too unmanageable.[21] Although this is purely an expert opinion process, indicators rated 8 or 9 in a RAND method have been found to be reproducible if rated by a panel composed of similar experts.[20]

Questionnaire compilation

After a literature review, a list of statements relating to the definition of occupational asthma was compiled. In addition a list of indicators relating to the resources a specialist occupational asthma clinic should be expected to provide was developed. The questionnaires were finalised after being reviewed by two occupational asthma specialists who were not included in the panel.

A total of 42 indicators were eventually compiled (14 for the definition of occupational asthma and 28 for resources required to run a specialist occupational asthma clinic).

Expert panel formation

The panel was identified as all members of the UK expert group GORDS (Group of Occupational Respiratory Disease Specialists), who were actively running NHS occupational lung disease clinics. It was felt that this group would provide a representative sample of all occupational asthma physicians in the UK.

Round 1: Postal round

The list of indicators and the rating scale were sent to panellists by post. Panellists were asked, without reference to each other, to rate the indicators.

Round 2: Expert Panel meeting

A panel meeting was scheduled to discuss, revise and re-rate the criteria face-to-face. The meeting was chaired by a moderator with previous experience of the RAND appropriateness method, but with no experience in occupational lung disease. The chairperson sought to resolve disagreement rather than attempting to force agreement. At the meeting the group's response to each indicator, together with each individual's own responses from round 1, were fed back to each panellist. This allows each participant to review their initial ranking in relation to their peers, although it was stressed that they did not need to conform to the group view. After a discussion of the relevant issues the questionnaire was re-rated.

Scoring responses

Rating scales to assess each indicator were developed using continuous integer scales of 1–9; with 1 denoting that the indicator was absolutely unnecessary/unimportant and 9 meaning it was absolutely necessary/important. Indicator ratings of 7, 8 or 9 were considered necessary, 4, 5 or 6 equivocal, and 1, 2 or 3 were considered unnecessary. At the subsequent expert panel meeting, these classifications were considered insufficiently sensitive and were redefined as detailed below (tables 1 and 2).

Table 1 Final rating scales and definitions used for defining occupational asthma

Rating scale	
1	Completely disagree
2, 3	May be true in occasional circumstances
4, 5, 6	Equivocal, unproven or undecided
7, 8	Generally true with some exceptions
9	Agree without reservation

Table 2 Final rating scales and definitions used to assess the necessity of resources required to run a specialist occupational asthma clinic

Rating scale	
1	No relevance to occupational asthma
2, 3	Not routinely required
4, 5, 6	May be useful but not a necessity
7, 8	Must be available
9	Absolute necessity in all patients

Consensus was defined as a panel median of 7 or more without disagreement, with disagreement being defined as where at least 33% of the panel members rated in both the upper (7, 8, 9) and lower tertiles (1, 2, 3).[17 19] All analyses are based on second round ratings (after the face-to-face meeting).

RESULTS

Nine panellists completed both the questionnaire and panel meeting rounds of the process, which represented 75% of suitable panellists. One panel member was unable to attend the face-to-face meeting and hence was not able to contribute to the final analysis.

Of the 42 indicators rated by the panel in the second round, 28 (67%) achieved consensus (median of 7–9 without disagreement).

Consensus was reached for 10 out of 14 (71%) of the indicators for defining occupational asthma (table 3) and the panel ''agreed without reservation'' regarding four of these indicators. One of the indicators was considered to be ''equivocal, unproven or undecided'' and one was classified as ''may be true in occasional circumstances''. There was disagreement over two of the indicators for the definition of occupational asthma.

Of the 28 indicators chosen for the resources required to run a specialist occupational asthma clinic, consensus was achieved for 18 (64%), with two being considered as an absolute necessity in all patients and 16 as ''must be available'' (table 4). Six of the indicators were classified as ''may be useful but not a necessity'' and four were considered to be either ''no relevance to occupational asthma'' or ''not routinely required''. There was no disagreement for any of the indicators used for resources required to run a specialist asthma clinic.

DISCUSSION

Diagnosing occupational asthma on history alone is not considered acceptable and is more reliable for the exclusion rather than the confirmation of occupational asthma.[22] However, in the UK there is no accepted guidance relating to the objective measures that should be available to physicians running specialist occupational asthma clinics. The outcomes of this exercise which specifically targeted the area of definition and assessment tools are complementary to the BOHRF

Table 3 Median panel scores for indicators relating to the defining occupational asthma

Median panel score	
9	Occupational asthma is defined as asthma induced by exposure in the working environment to airborne dusts, vapours or fumes
	Occupational asthma is defined as asthma induced by exposure in the working environment to airborne dusts, vapours or fumes, with or without pre-existing asthma
	Respiratory sensitisation can sometimes occur to agents for which an immune mechanism has not been identified
	For some agents both immunological and non-immunological mechanisms may be involved (eg, diisocyanates)
8	Occupational asthma encompasses sensitiser-induced asthma and acute irritant induced asthma (RADS)
	Sensitiser-induced occupational asthma occurs following a latency period.
	Acute irritant induced asthma (RADS) is a type of occupational asthma where there is no latency period and no immunological sensitisation
	The term RADS should only be used when a single high exposure episode has occurred
	Work-related asthma includes sensitiser-induced occupational asthma, acute irritant induced asthma (RADS) and aggravation of pre-existing asthma
	If low dose irritant-induced asthma exists I would include it in work-related asthma
5	Recurrent low-dose, irritant-induced asthma is a condition I sometimes diagnose*
	Occupational asthma can occur following transdermal exposure to a sensitising agent
3	The term ''occupational asthma'' should be reserved for cases where a sensitisation process is implied*
2	Acute irritant-induced asthma should be reserved for pre-existing asthma made worse by work exposures rather than caused by work exposures

*Indicates disagreement.

document[1] which has recently and extensively explored evidence base for risk factors, diagnostic procedures, management and prevention methods in occupational asthma.

Eighteen essential resources required to run a specialist occupational asthma clinic were agreed upon. It is hoped that this list will form the basis of a subsequent advisory document for investigational centres for occupational lung disease in the UK. These resources may appear similar to those needed for a general respiratory clinic. However, considerable skill and experience is necessary to manage safely some of the essential resources, such as specific inhalation challenge tests. Furthermore, the opinion of an experienced clinician is superior to computerised analysis of serial peak flow measurements. This is likely to be particularly relevant when distinguishing between ''work aggravated asthma'' and occupational asthma. It is interesting that the panel regarded formal training in occupational medicine as being useful but not essential. Pre-bronchodilator FEV_1 and FVC (shown in surveys of occupational asthma to be lacking in sensitivity and specificity[1]) achieved a median panel score of 9, whereas specific inhalation challenge in the laboratory was given a median panel score of 7. It is likely that bias has been introduced by the availability of these resources at the panellists' sites. The availability in the UK of the 18 indicators that were perceived as best practice by the expert panel is unknown. It is accepted fully that this has fundamental implications in terms of funding of specialist units and accessibility of the units to all possible cases of occupational asthma in the UK.

Reaching a consensus on the definition of occupational asthma proved more challenging. However, the results of this aspect of the exercise may help to clarify the use of terminology that has been used interchangeably in the past. The panel were able to agree that ''occupational asthma is defined as asthma induced by exposure in the working environment to airborne

Table 4 Median panel scores for indicator relating to the investigation of occupational asthma

Median panel score	
9	Pre-bronchodilator FEV_1 as a percent of predicted
	Pre-bronchodilator FVC as a percent of predicted
8	Peak flow monitoring and plotting of results
	OASYS II analysis of peak flow records
	Non-specific provocation challenge in the clinical laboratory
	Specific IgE to a wide variety of occupational agents
7	Carbon monoxide transfer factor (TLCO)
	Transfer coefficient (KCO)
	Non-specific provocation challenge serially at work and away from work
	Specific occupational challenge in the clinical laboratory
	Chest *x* ray
	Total IgE
	Skin prick testing to common environmental allergens
	Workplace visit by a clinician
	Workplace challenge with peak flow monitoring/spirometry
	Standard haematology/biochemistry (LFT, TFT, CA^{2+})
	Access to a toxicology database
	RAST testing to common environmental allergens
4, 5, 6	Measurement of workplace exposure levels
	Assessment of vocal cord dysfunction
	Portable lung function logging device
	Standardised occupational history form
	Training in occupational medicine to at least Dip Occ Med
	Total lung capacity (TLC)
3	Sputum eosinophils
2	Exhaled nitric oxide (NO)
	Expired carbon monoxide (CO)
	Exhaled breath condensate for analysis of inflammatory markers

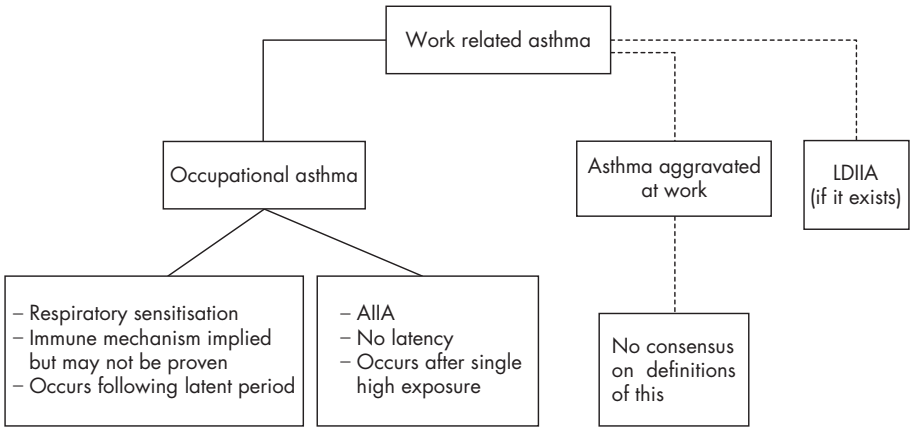

Figure 1 Proposed categorisation of work related asthma.

dusts, vapours or fumes'', which is in agreement with the definition of occupational asthma proposed by Newman-Taylor[5] and seems testament to the durability of this definition. It was expanded at the face-to-face meeting to include ''with or without pre-existing asthma'' and consensus was reached on this modified statement. This allows for the scenario of a worker with pre-existing asthma developing new sensitisation to something they are exposed to within the workplace (in other words occupational asthma superimposed on previous non-occupational asthma).

Consensus was reached that occupational asthma should include what has previously been known as RADS (although the panel preferred the term ''acute irritant-induced asthma''). This is consistent with definitions proposed by Vandenplas and Malo[23] and by the BOHRF guidelines for occupational asthma.[1] A further important issue was that the panel reached a consensus that respiratory sensitisation can occur where an immune mechanism may not be found. Finally, the panel agreed that the term ''work-related asthma'' should include occupational asthma, acute irritant-induced asthma and workers with pre-existing asthma aggravated by work (by whatever mechanism).

The possibility of extending the spectrum of irritant induced asthma further to include the onset of asthma following repeated exposure to low concentrations of irritants in the workplace (''low-dose irritant-induced asthma'') has been suggested,[24 25] although supporting evidence for its existence is weak. This definition would also blur the distinction based on latency, because repeated exposures up to a threshold level would be required before symptoms ensue. There was disagreement among the panel over whether this entity exists, but if it were proven then the panel felt it should be included in the term ''work-related asthma''. The panel also disagreed that occupational asthma should be limited to cases where a sensitisation process is implied. Hence, the overall message is that occupational asthma involves sensitiser-induced asthma and acute irritant-induced asthma, but not low-dose irritant-induced asthma or work-aggravated asthma. A summary of these definition outcomes is given in figure 1. This figure has similarities to the phenotypic entities of occupational asthma as suggested by Bernstein *et al*,[9] but the central difference in our consensus surrounds the debate over whether or not low-dose irritant-induced asthma exists.

It is recognised that this clarifying of terminology does not really help with the difficult clinical decisions of whether it is reasonable to leave someone in an exposed area and when cessation of exposure should be aggressively pursued. However, it is hoped that the outcome of this exercise will help improve uniformity of definition across the UK, although it is likely that some local variation will still occur. The authors hope that the outcome of this exercise will also set a template of the minimum criteria for establishing a specialist service in occupational asthma within the UK.

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Main messages

- There is no internationally agreed definition of occupational asthma, and guidance regarding resources that should be available to physicians running specialist occupational asthma clinics is lacking.
- This exercise may help to improve uniformity of definition and investigation of occupational asthma across the UK.

Policy implications

- Eighteen essential resources required to run a specialist occupational asthma clinic were agreed upon. It is hoped that this list will form the basis of a subsequent advisory document for investigational centres for occupational lung disease in the UK.

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